Attached hereto is an executed Terminal Disclaimer.

Accordingly, withdrawal of the obviousness-type double-patenting rejection is requested respectfully.

II. On page 3 of the Office Action, claims 1-12 were rejected under 35 U.S.C. § 112, first paragraph. The Examiner alleged that the claims were not enabled.

The rejection is traversed for the following reasons.

The first paragraph of 35 U.S.C. §112 requires that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention. Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples (*In re Wright*, 999 F.2d 1557, 27 USPQ2d 1510 (Fed Cir. 1993). The enablement requirement is met if the description enables any mode of making and using the claimed invention (*Engel Industries, Inc. v. Lockformer Co.,* 946 F.2d 1528, 20 USPQ2d 1300 (Fed. Cir. 1991).

Applicants submit that the present claims are enabled by the specification as filed for the reasons set forth below.

By way of background, the administration of AAV by routes that offer more direct access to the circulation or target tissue, such as non-parenteral administration, was known in the art prior to the filing date of the instant application. For example, U.S. Patent No. 6,162,796, filed 27 September 1995, describes a method of delivering DNA using AAV that was administered intra-arterially. In addition, U.S. Patent No. 6,180,613, filed 6 June 1995,

teaches stereotactic administration of AAV into the brain and U.S. Patent No. 6,211,163, claiming benefit to 18 January 1996, describes a method of intravenous delivery of recombinant AAV.

Thus, the state of the art teaches successful non-parenteral administration of AAV to deliver genes to a host.

The instant application demonstrates the successful administration of AAV by one of the more harsh routes of delivery of a pharmaceutical to a host. Oral delivery of a treatment compound requires that the compound, in part, survive the acidic environment of the stomach. The experimental results provided in the instant application demonstrate that the AAV vector, which is known to be very stable under extreme conditions, survives exposure to the acidic environment of the stomach, traverses into the small intestine, resulting in expression of the transgene.

Further evidence that AAV infects a wide range of cells is provided in Dreizin et al. Vopr. Varisol. 1:82-89, 1981, English translation of abstract attached hereto, which teaches that AAV in green monkeys infects a wide range of cells including conjunctiva, tonsils, rectal specimens, spleen, liver, intestines and kidney.

During et al., Nature Med. 4:1131-1135, 1998, copy attached hereto, demonstrate the feasibility of oral AAV administration as a means to obtain long-term gene expression in the gastrointestinal system. During et al. teach that orally administered AAV infected a variety of cells in the small intestine, as well as cells of the stomach, with the highest level of expression in the stomach, duodenum and proximal jejunum (page 1132). The disclosure of During et al. supports the enablement of the current claims based on the application as filed.

Hence, there is ample evidence of record that the state of the art recognized that AAV is a suitable vector for delivering a variety of genes. Moreover, a variety of cells are suitable targets of AAV and can be infected thereby. The instant application teaches that the oral administration of AAV leads to the successful transformation of cells within the gastrointestinal tract.

It is believed the Examiner has not provided a reasonable basis for concluding that the instant invention is not enabled for AAV vector-mediated gene expression in the gut. The evidence of record teaches a large number of cells being transformed, different genes being delivered and a variety of routes being employed.

There is no basis to conclude that any transgene that does not express a protein cannot be expressed by AAV.

Hence, it is concluded that the Examiner has not provided a prima facie case of non-enablement.

The evidence of record and the state of the art clearly establish the claims are fully enabled. Accordingly, withdrawal of the rejection is in order.

III. On page 6 of the Office Action, claim 12 was rejected under 35 U.S.C. § 112, second paragraph. The Examiner raised an issue with respect to the phrases, "and promoter system" and "said DNA segment."

The rejection is traversed for the following reasons.

The suggestion of the Examiner has been accepted and proper antecedent basis now is found in claim 12. Accordingly, withdrawal of the rejection is in order.

CONCLUSION

Applicant has taken steps to advance prosecution of the instant application and the claims now are in condition for allowance. Reexamination, reconsideration, withdrawal of the rejections and early indication of allowance are solicited earnestly. If any questions remain unresolved, the Examiner is urged to contact the undersigned at the local exchange noted hereinbelow.

The Commissioner is authorized to charge Deposit Account No. 18-2220 for any fees that might be precipitated by the filing of the instant Amendment.

Respectfully submitted,

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Page 2, fourth and fifth paragraphs:

[Figure 1 is a graph] Figures 1A-1C are graphs showing plasma glucose and animal weight following acute lactose challenge and lactose-only diet. [A. The] Figure 1A shows the change in plasma glucose following the ingestion of lactose in overnight fasted rats. Rats were studied 1 week following AAVlac or PBS administration. [B. The] Figure B shows the results of oral lactose challenge [was] repeated after 14 days on the lactose diet. [C. The] Figure 1C shows the weight of rats at baseline, 1 week and 2 weeks following a 14 day lactose and water diet. The diet commenced 1 week following oral AAVlac or PBS treatment.

[Figure 2. A. The] Figures 2A-2B. Figure 2A shows the change in plasma glucose following the ingestion of lactose in overnight fasted rats, which were challenged 120 days following a single peroral dose of AAVlac or PBS. [B. The] Figure 2B shows the weights of rats at baseline, 1 week and 2 weeks following a 14 day lactose and water diet. The diet commenced 120 days following oral AAVlac or PBS treatment.

12. (Amended) The method of claim 1, wherein said [DNA segment] non-AAV gene of interest comprises a β-galactosidase gene operatively linked to a [and] promoter [system].